REMARKS/ARGUMENTS

Status of the Prosecution.

This response is to the Office Action dated February 9, 2004, which was in response to the amendments filed with the Request for Continued Examination (RCE) filed November 6, 2003.

Claims 27-50, 66-68, and 72-86 are pending. By the above amendment, non-elected claims 1-26, 51-65, and 69-71 have been cancelled without prejudice or disclaimer to reduce issues. Claims 27-50, 66-68, and 72-81, which related generally to the subject matter of elected claims 82-85, remain withdrawn as directed to non-elected inventions. Claims 82-85 are presently under examination. Claim 86 is newly presented herein. Support for the newly presented claim can be found throughout the specification.

Claims 82 and 84 are amended herein to correct typographical errors and to better clarify the invention for the examiner. It is believed that the claims as amended and the new claim are in condition for allowance.

Notations and Objections Have Been Addressed.

The applicants thank the examiner for the notation with respect to the Information Disclosure Statement (IDS) filed January 29, 2001 and confirm for the record that sheet 1 of the Information Disclosure Citation form accompanying the IDS in fact lists all of the references cited. In other words, the indication that such sheet is "sheet 1 of 3" appears to have been a typographical error.

In addition applicants again acknowledge that formal drawings will be required upon allowance.

The Claims are not Anticipated under 35 U.S.C. § 102(b) by Mazer *et al.*

Claims 82 -85 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Mazer *et al.* Applicants respectfully traverse this rejection. The amendments have clarified that the claimed compound does not directly stimulate the protease activity, as the examiner apparently understood (page 4 of the Office Action, lines 2-5). Independent claims 82 and 84 now clearly reflects that the stimulation of the protease activity is due to a signal transduced

by the cellular receptor, and that the claimed compound modulates this signal. In contrast Mazer *et al.* teach calcium as a dietary supplement. There is no explicit or inherent teaching that Mazer's calcium supplement is a compound that modulates a signal as in the claimed invention.

In addition, applicants point out that a calcium ion (Ca^{2+}) is not a "compound" at all, as that term is used in the art or in the instant specification. A compound by definition cannot be an ion.

Thus, the compositions of Mazer *et al.* cannot be said to anticipate the amended claims for at least two reasons: (1) because they are not compounds, and (2) because they do not bind to the cellular receptor or transduce the signal which stimulates the activity of the protease. Accordingly, withdrawal of the rejection of claims 82-85 under 35 U.S.C. § 102(b) is again respectfully requested. Since the cited reference also cannot be said to suggest the presently claimed invention, the claims are allowable over the prior art.

The Claims Are Definite Within the Meaning of 35 U.S.C. § 112, second paragraph.

Claims 82-85 stand newly rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Applicants respectfully traverse this rejection. The Office Action states that the compound acts downstream from any extracellular receptor activation. The claims as amended clarify that the compounds act as modulators of the cellular receptors of the invention. The nexus is clearly established between the modulation of the receptor and the activity of the compound, as the amendment clarifies that the downstream signal results in the activation of the protease, and that it is not a direct action of the claimed compound. See, for example, the disclosure on page 18 wherein it is stated at line 1 "One example is to use calpain cleavage to report ***intracellular release of Ca^{++} due to GPCR or ion channel activation***. . ." The claims are therefore definite, containing a proper nexus between interaction of the compound with the receptor and the activation of the protease, and further use the term "modulation" in a clear way to indicate that activity can be either increased or decreased. Furthermore, with respect to the term "modulate", the disclosure on page 12 states that "This method is useful to determine compounds that modulate a receptor by measuring changes of the normal amount of gene product produced by a known amount of a

ligand. ***If the compound is antagonist, the amount of gene product will decrease, while an agonist compound may increase the level of gene transcription.***"

In view of the foregoing, applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Conclusion:

The amendments and remarks herein are believed to be fully responsive to the Office Action. Applicants respectfully assert that all claims are now in condition for allowance. An early and favorable Notice to that end is earnestly solicited. To resolve any outstanding issues prior to allowance of the claims, the examiner is invited to contact the applicants' undersigned representative by telephone at 215-557-5986.

Respectfully submitted,

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